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Original Article

Psychiatry/Mental Health Section

# Correlation of HDL and LDL Cholesterol with Severity of Depression: A Cross-sectional Study

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## ABSTRACT

**Introduction:** Depression is one of the leading causes of morbidity worldwide. It can impact various biomarkers, including proteins, monoamines, and lipids. Lipids play a critical role in regulating cellular function by influencing transport, anchoring, and providing structural support. The present study aimed to explore any correlation between lipid profiles and depression.

**Aim:** To investigate the correlation between different lipid profile parameters (serum triglycerides, total cholesterol, serum High-density Lipoproteins (HDL), and Low-density Lipoproteins (LDL) levels) and the severity of depression.

**Materials and Methods:** A hospital-based, cross-sectional study was conducted at the Department of Psychiatry, Faculty of Medicine and Health Sciences, SGT University, Gurugram, Haryana, India, from June 2020 to June 2021. A total of 200 participants aged 18-65 years, diagnosed with depression according to the ICD-10 classification, were enrolled. Clinical assessments were conducted, and the Hamilton Depression Rating Scale (HAM-D) (17 items) and Beck's Depression Inventory II (BDI II) (21-item scale) were used. Lipid parameters were obtained from fasting blood samples. The Wilcoxon's-Mann-Whitney U test was applied to assess the association between gender distribution and lipid profiles. Spearman's correlation test was used to analyse the correlation between HAM-D and BDI scores with lipid profiles. Statistical significance was set at a p-value ≤0.05.

**Results:** The mean age of the participants was 36.05±11.24 years. Correlations between HAM-D levels and lipid profiles revealed that all lipid parameters, except for HDL (which showed a negative correlation), were positively associated with HAM-D scores. These correlations were statistically significant (p≤0.05). Similarly, a positive correlation was observed between all lipid levels and BDI scores, except for HDL, which exhibited a negative correlation. These correlations were also statistically significant (p≤0.05).

**Conclusion:** Higher levels of LDL cholesterol were found to be associated with elevated depression rating scale scores and increased susceptibility to depression. On the other hand, HDL cholesterol demonstrated protective effects against depression. Adopting a healthy lifestyle, implementing dietary measures, and addressing stressors promptly may help prevent depressive symptoms.


**Keywords:** Affective disorders, Depression rating scales, High-density lipoproteins, Lipid profile, Low-density lipoproteins, Stress

## INTRODUCTION

Depression is one of the most diagnosed mental disorders in primary care settings [1]. By 2030, unipolar depression is predicted to be the second leading contributor to the global burden of disease [2,3]. Depression shares common aetiological factors with other non communicable illnesses and can amplify the disease burden as co-morbidity or as a consequence of it, thus having a significant impact on individuals, families, and societies [4]. The role of cholesterol, whether it is HDL or "good" cholesterol, and LDL or "bad" cholesterol, is highlighted in certain cardiac and neurological diseases, and their association with mood disorders is evident [5]. Increased Body Mass Index (BMI) and obesity have been linked to mood disorders, and mood disorders such as depression or recurrent depression have been associated with obesity [6]. Furthermore, anxiety spectrum disorders including panic disorder, obsessive-compulsive disorders, and phobias have been found to have elevated serum cholesterol levels [7-9].

Lipids are important constituents in cell functioning and play a crucial role in various cellular processes, including supporting and binding the cell membrane. While protein dysfunction has been highlighted in relation to monoamines and neuroendocrine mechanisms, which are in turn related to mood disorders, lipids also have a significant effect on neurotransmission, signal transduction, and neuroplasticity [5].

Chronic stress and depression can lead to inflammatory reactions and changes in lipid metabolism, resulting in an increase in cholesterol levels [9]. Although the use of cholesterol as a dietary supplement in depression can be debated, it is unlikely to have beneficial effects, and the credibility of this experimental treatment raises further questions. However, cholesterol-reducing drugs such as statins can be employed. Studies conducted with lovastatin in combination with the antidepressant fluoxetine have shown a statistically significant reduction in HAM-D scores compared to controls [10,11]. A systematic review and meta-analysis conducted by Parsaik AK et al., also suggest that statin use is associated with a lower risk of depression [12]. Therefore, the estimation of serum cholesterol levels and their effects on the severity of depression and treatment outcomes are essential.

Therefore, the present study aimed to determine the correlation of serum lipid profile with depression and to highlight the correlation between various parameters of the lipid profile (serum HDL, LDL, triglyceride, and total cholesterol levels) and the severity of depression.

## MATERIALS AND METHODS

It was a hospital-based, cross-sectional study conducted at the Department of Psychiatry, Faculty of Medicine and Health Sciences, Gurugram, Haryana, India from June 2020 to June 2021. The study was approved by the Institutional Research Committee and Institutional Ethics Committee (Number: IEC/FMHS/MD/S/2020-1). Written informed consent was obtained from each participant after explaining the study to them.

**Sample size calculation:** Using the formula 4 pq/$d^2$, based on a previous study by Sagar R and Selvakumar N on the prevalence of depression, the prevalence 'p' was taken as 15%, q=100-p=85, and d (absolute precision) was taken as 5. Therefore, 4 pq/$d^2$=4×15×85/25 [13].

Hence, the final sample size was calculated to be 204. However, 200 patients were enrolled. The patients were diagnosed with depressive disorder according to the International Classification of Disease-10 (ICD-10) [14].

**Inclusion criteria:** Patients who were newly diagnosed with depressive disorder, i.e., first episode of depression (mild, moderate, and severe), were included. The age group focused on was 18 to 70 years. The severity of depression was assessed using the Hamilton Depression Rating Scale (HAM-D) [15,16] and Beck's Depression Inventory II (BDI II) [17,18].

**Exclusion criteria:**

- Patients with co-existing major psychiatric disorders (schizophrenia, bipolar disorder).
- Patients with intellectual disability.
- Patients taking any lipid-lowering drugs.
- Pregnant females and lactating mothers.

### Study Procedure

**Semi-structured proforma:** Used to record the socio-demographic details of the patients, such as age, sex, education, area of residence, family income, lifestyle, and stressors.

**Hamilton Depression Rating Scale (HDR-S):** A 21-item clinician-rated scale used to assess the severity and change in depressive symptoms. Scoring is based on the first 17 items, with scores ranging from 0 (no presence) to 4 (significant presence) for eight items, and scores ranging from 0 to 2 for nine items [15]. The scale has a sensitivity of 86.4% and a specificity of 92.2%. Inter-rater reliability for HAM-D total scores ranges from 0.82 to 0.98 [16].

**Beck's Depression Inventory II (BDI):** A 21-item self-reporting questionnaire used to assess depression severity. Each question is graded on a scale of 0 to 3, with higher overall scores indicating more severe depressive symptoms [17]. The internal consistency of the scale, measured using Cronbach's α coefficient, was α=0.78 for the cognitive dimension, α=0.77 for the somatic dimension, and α=0.70 for the affective dimension [18,19].

Patients were advised to come after overnight fasting for lipid profile estimation within two weeks. Lipoprotein levels were determined using the National Cholesterol Education Program Adult Treatment Panel (NCEP ATP III) classification of total cholesterol, LDL, and HDL Cholesterol (mg/dL) [20].

## STATISTICAL ANALYSIS

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS 22.0) software. Descriptive statistics were analysed using the mean, Standard Deviation (SD), numbers, and percentages. For inferential statistics, the Wilcoxon-Mann-Whitney U test was applied to determine the association between gender distribution and lipid profile. Spearman's correlation test was used to identify correlations between HAM-D and BDI scores with the lipid profile.

## RESULTS

The mean age of the participants was 36.05±11.24 years. The majority of the patients 65 (32.5%) belonged to the age group of 31-40 years. Approximately half of the patients 99 (49.5%) were male. The majority of them were married 148 (74%) and resided in urban areas 116 (58%). Active stressors were reported by 126 (63%) of patients [Table/Fig-1]. No significant association was found between gender and lipid profile, including cholesterol (p=0.775), triglyceride (p=0.404), HDL (p=0.577), LDL (p=0.491), and VLDL (p=0.498) [Table/Fig-2].

| Variables | | N=200 | |
|---|---|---|---|
| | | n | (%) |
| Age | ≤20 years | 17 | 8.5 |
| | 21-30 years | 58 | 29 |
| | 31-40 years | 65 | 32.5 |
| | 41-50 years | 40 | 20 |
| | 51-60 years | 15 | 7.5 |
| | 61-70 years | 5 | 2.5 |
| Sex | Male | 99 | 49.5 |
| | Female | 101 | 50.5 |
| Education | Illiterate | 9 | 4.5 |
| | 10th std | 43 | 21.5 |
| | 12th std | 63 | 31.5 |
| | Graduate | 76 | 38 |
| | Postgraduate | 9 | 4.5 |
| Occupation | Employed | 99 | 49.5 |
| | Unemployed | 97 | 48.5 |
| | Retired | 4 | 2 |
| Locality | Rural | 84 | 42 |
| | Urban | 116 | 58 |
| Lifestyle | Sedentary | 112 | 56 |
| | Healthy | 88 | 44 |
| Marital status | Married | 148 | 74 |
| | Unmarried | 52 | 26 |
| Stressor | Present | 126 | 63 |
| | Absent | 74 | 37 |

**[Table/Fig-1]:** Socio-demographic details of patients.

| Lipid profile (mg/dL) | Gender | | Tests | p-value |
|---|---|---|---|---|
| | Male (Mean±SD) | Female (Mean±SD) | | |
| Total cholesterol | 197.26±42.36 | 198.98±42.82 | W=0.286 | 0.775 |
| Triglyceride | 117.23±31.57 | 127.97±79.87 | W=657.5 | 0.404 |
| HDL | 50.54±38.38 | 46.67±10.76 | W=228.5 | 0.577 |
| LDL | 106.63±28.36 | 109.17±29.54 | W=717.0 | 0.491 |
| VLDL | 22.44±9.56 | 23.16±9.36 | W=721.5 | 0.498 |

**[Table/Fig-2]:** Association between gender and lipid profile.
*HDL: High density lipoproteins; LDL: How density lipoproteins; VLDL: Very low density lipoproteins.
W: Wilcoxon-Mann-Whitney U test was applied. p-value was statistically significant at p=0.05

The mean HAM-D and BDI scores of the patients were 14.53±3.67 and 23.50±7.08, respectively [Table/Fig-3]. There was a negative correlation between HAM-D scores and HDL (r=-0.2, p<0.027), while positive correlations were observed between other lipid levels and HAM-D scores, including cholesterol (r=0.8, p=<0.001), triglyceride (r=0.4, p<0.001), LDL (r=0.7, p<0.001), and VLDL (r=0.2, p<0.001) [Table/Fig-4].

| Depression | n (%) |
|---|---|
| HAM-D score (Mean±SD) | 14.53±3.67 |
| **HAM-D category** | |
| Mild | 14 (7.0%) |
| Moderate | 121 (60.5%) |
| Severe | 61 (30.5%) |
| Extremely severe | 4 (2.0%) |
| BDI score (Mean±SD) | 23.50±7.08 |

| BDI category | |
|---|---|
| Mild | 16 (8.0%) |
| Borderline | 17 (8.5%) |
| Moderate | 121 (60.5%) |
| Severe | 44 (22.0%) |
| Extreme | 2 (1.0%) |

**[Table/Fig-3]:** Frequency of HAM-D and BDI scores of patients.
HAM-D: Hamilton depression rating-scale; BDI: Beck's depression inventory

| Correlation | Spearman's correlation coefficient | p-value |
|---|---|---|
| Cholesterol (mg/dL) vs HAM-D score | 0.8 | <0.001 |
| Triglyceride (mg/dL) vs HAM-D score | 0.4 | <0.001 |
| HDL (mg/dL) vs HAM-D score | -0.2 | 0.027 |
| LDL (mg/dL) vs HAM-D score | 0.7 | <0.001 |
| VLDL (mg/dL) vs HAM-D score | 0.2 | <0.001 |

**[Table/Fig-4]:** Correlation between HAM-D scores and lipid profile.
HAM-D: Hamilton depression rating scale; HDL: High density lipoproteins; LDL: Low density lipoproteins; VLDL: Very low density lipoproteins

A negative correlation was found between BDI scores and HDL (r=-0.1, p=0.033), while positive correlations were observed between other lipid levels and BDI scores, including cholesterol (r=0.7, p=<0.001), triglyceride (r=0.4, p<0.001), LDL (r=0.7, p<0.001), and VLDL (r=0.2, p<0.002) [Table/Fig-5].

| Correlation | Spearman's correlation coefficient | p-value |
|---|---|---|
| Cholesterol (mg/dL) vs BDI score | 0.7 | <0.001 |
| Triglyceride (mg/dL) vs BDI score | 0.4 | <0.001 |
| HDL (mg/dL) vs BDI score | -0.1 | 0.033 |
| LDL (mg/dL) vs BDI score | 0.7 | <0.001 |
| VLDL (mg/dL) vs BDI score | 0.2 | 0.002 |

**[Table/Fig-5]:** Correlation between BDI scores and lipid profile.
BDI: Beck's depression inventory; HDL: High density lipoproteins; LDL: Low density lipoproteins; VLDL: Very low density lipoproteins

## DISCUSSION

The mean age of the participants in the present study was 36.05±11.24 years. The higher participation of individuals in their 30's and 40's was consistent with the typical age range for the first episode of depression [21]. These findings align with previous studies conducted in India, which also included participants aged 18-65 years, with a mean age of 32.47 years [21,22]. The inclusion of a homogeneous cohort of individuals with depression, with an almost equal distribution of male and female participants, allows for generalisation of the findings to the wider community. Approximately half of the patients (49%) were male, and the majority were married (74%) and residing in urban areas (58%). Most patients (63%) reported having an active stressor.

There was no statistically significant difference in mean HDL (mg/dL) scores based on gender distribution. However, Kim EJ et al., reported that LDL levels were associated with the risk of depression, particularly in boys [23]. It is believed that males may have higher cholesterol levels due to different stressors and additional substance usage. However, the present study suggests that lipid levels were equally deranged in both males and females.

In the present study, both the HAM-D and BDI rating scales were utilised to assess depression. The HAM-D was administered by clinicians, and the evaluation with this instrument can vary depending on the expertise of the clinician. On the other hand, the BDI is a self-reporting scale, and patients may intentionally exaggerate or conceal their depressive symptoms. The advantage of using both subjective and objective scales was to obtain a comprehensive assessment of patients, considering both somatic and cognitive symptoms.

When categorising the participants based on the severity of depression using the HAM-D and BDI scales, it was observed that the majority of the participants in the present study had moderate depression, followed by severe depression. The severity of depression may be associated with deranged lipid levels, as Wagner CJ et al., found that serum LDL levels were higher in patients with Major Depressive Disorder [24]. However, further investigation is needed to examine the relationship between increased LDL levels (in terms of units, such as mg/dL) and the severity of depression (i.e., moderate, moderately-severe, or severe).

In the present study, a negative correlation was observed between depression and HDL cholesterol, suggesting a protective effect of HDL cholesterol against depression. The presence of depressive cognition in patients with elevated levels of LDL cholesterol supports the notion of negative effects of "bad" cholesterol. Previous studies have demonstrated an inverse relationship between HDL levels and depression [25,26]. However, Jia QF et al., reported high levels of HDL in patients with depression [27]. Other authors have reported mixed findings regarding the association between serum cholesterol and depression [24,28,29]. Further clarification is needed to determine whether changes in serum lipids contribute to the development of depression or if depression leads to alterations in lipid profiles, or if there is simply a causal relationship.

However, more research is required to analyse the lipid pathways and the effects of lipids in relation to psychiatric illnesses, particularly mood disorders. Additionally, only a subgroup of patients in the present study demonstrated an association with altered lipid profiles, which suggests the possibility of defining patients according to subtypes based on lipids as a biomarker. Routine lipid testing may be recommended for individuals, although it would increase treatment costs. However, the role of lipids in the pathophysiology of depression and the action of drugs on certain receptors, which are composed of lipids, cannot be ignored.

### Limitation(s)

Strong emotions could have influenced the results, and it should be noted that the present study was cross-sectional, meaning that different results may be obtained in different time frames. The evaluation of family dynamics was not conducted, which could have provided further insights into the support system available within the family. Additionally, other confounding factors such as substance abuse, medication history, obesity, and dietary patterns were not determined, which could have further influenced the levels of depression.

## CONCLUSION(S)

Depressive individuals were found to have adverse plasma lipid patterns, characterised by higher levels of total cholesterol and LDL, as well as lower levels of HDL cholesterol. Based on these findings, it may be suggested to consider routine lipid measurements for patients. However, further research is needed to analyse the lipid pathways and understand the effects of lipids in relation to psychiatric illnesses, especially mood disorders. Moreover, it is important to note that only a subgroup of patients in the present study demonstrated a relationship with altered lipid profiles, indicating the potential to classify patients into subtypes based on lipid biomarkers.

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